

COMPOSITIONS AND METHODS FOR REGULATED PROTEIN EXPRESSION IN GUT

This application claims priority to Provisional Application Serial No. 60/188,796, filed March 13, 2000 and Provisional Application Serial No. 60/254,464, filed December 8, 2000.

TECHNICAL FIELD

This invention relates to regulatable production of proteins in the gut, and more particularly to nutrient regulated production of glucose-lowering factors from gut endocrine cells.

BACKGROUND

Peptides and proteins, by virtue of their conformational versatility and functional specificity, have been used in treating a host of diseases including diabetes, hemophilia, cancer, cardiovascular disorders, infectious diseases and arthritis (Russell C.S. & Clarke L.A. *Clin Gent* **55**(6):389 (1999); Ryffel B. *Biomed environ Sci* **10**:65(1997); Koths K. *Curr Opin Biotechnol* **6**:681 (1995); Buckel P. *Trends Pharmacol Sci* **17**:450 (1996)). Presently, more than two thirds of the approved biotech medicines are systemic protein drugs. With recent advances in the field of functional genomics, proteomics and genetic engineering, an increasing number of protein drugs are entering the biopharmaceutical market.

Originally, protein drugs were purified from animal tissues or human serum. Protein-based pharmaceuticals have gone through several stages of improvement to reach the current state of clinical application. For example, the biopharmaceutical industry now uses genetically engineered yeast and bacteria to manufacture recombinant human proteins (Scopes R.K. *Biotechnol Appl Biochem* **23**:197 (1996)). This groundbreaking technology has overcome the health risk and shortages that plagued the first generation of protein drugs, and has consequently improved the therapeutic value of proteins. However, despite these advances, broad usage of proteins as therapeutics is still hampered by difficulties in purifying recombinant proteins in active forms and the high cost of manufacturing procedures (Berthold W. & Walter J. *Biologicals* **22**:135(1994); Scopes R.K. *Biotechnol Appl Biochem* **23**:197 (1996)). Additionally, protein drugs face barriers to their entry into the body. When taken orally, they are susceptible to break down by enzymes in the